REMARKS

Claims 5-10, 21, 23, 24, and 26-29 are pending in this application. Claims 5, 8, 9, 10 and 21 have been amended to reflect the telephonic interview with the Examiner. Support for the term "pharmaceutical acceptable carrier" can be found throughout the specification, more specifically, page 4, line 5. No new matter has been added.

The issues outstanding in this application are as follows:

- Claims 5-10, 21, 23, 24 and 26-29 were rejected under 35 U.S.C. §103(a), in which the Examiner alleges that the claimed subject matter is unpatentable over Teng et al. in view of Britigan, Morianga Milk Inc. (JP 07-233086) and De Lacharriere et al.

Applicants respectfully traverse the outstanding rejections and objections, and applicants respectfully request reconsideration and withdrawal thereof in light of the amendments and remarks contained herein.

35 U.S.C. §103(a)

Claims 5-10, 21, 23, 24 and 26-29 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over the primary reference Teng et al. in combination of the above-listed references.

The Examiner states that Teng et al. teaches a method of treating dermal inflammatory disorder comprising the step of administering a pharmaceutically effective amount of a lactoferrin product. The Examiner also states that Teng et al. does not teach the treatment of the particular dermal disorder or the employment of biological analog or fragments of lactoferrin. The Examiner states that Britigan teaches that lactoferrin is known to be useful as an anti-inflammatory agent and that Morinaga Milk Inc. teaches that lactoferrin or its derivatives are known to be useful for treating various skin disorders. The Examiner also states that De Lacharrier et al. teaches that TNF antagonists, lactoferrin, are known to treat or prevent skin inflammation. Applicants traverse.

The MPEP sets forth the guidelines to establish a prima facie case of obviousness under 35 U.S.C. § 103 (MPEP § 2143.3). Three basic criteria must be met to establish a prima facie case of obviousness. The three criteria are:

> 1) a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
>
> 2) a reasonable expectation of success; and
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> 3) the prior art references must teach or suggest all the claim limitations.

In view of the above criteria, Applicants assert that the Office has not established a *prima facie* case of obviousness to reject the claims under 35 U.S.C. § 103 in light of the above criteria. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438, (Fed. Cir. 1991). A *prima facie* case necessitates disclosure of the source for either a suggestion or motivation to modify a reference to produce the present invention, and a reasonable expectation of success of producing the present invention. A *prima facie* case must be established by evidence rather

than conjecture. *Ex parte Yamamoto*, 57 USPQ2d 1382, 1383, 1384 (CCPA 2000). In the present case, it is mere conjecture on the part of the Office that one of skill in the art would be able use the lactoferrin composition in Teng et al. in combination with the lactoferrin compositions described in Britigan et al., Morinaga Milk Inc., and the TNF α antagonists described in De Lacharriere to develop the lactoferrin composition of the present invention to treat an allergen-induced inflammatory response.

The present invention is drawn to the use of lactoferrin to prevent or treat an allergen-induced inflammatory response. Those of skill in the art realize that the mechanisms involved in an allergen-induced immune response differ from an immune response resulting from an insult by a pathogenic agent, such as bacteria or viruses. Inflammation that occurs via a pathogenic agent is typically a result of endotoxin toxicity. Endotoxins are toxins that are released from the pathogen. An endotoxin is **not an innocuous agent**; it is toxic to the cell and triggers phagocytes to release cytokines that produce local or systemic symptoms. An allergen-induced inflammatory response, on the other hand, results from the immune system responding to an **innocuous agent**.

Applicants assert that Teng et al., and Britigan et al., do not teach or suggest the use of lactoferrin to treat an allergen-induced inflammatory response. The present application, on page 3, lines 20-21, indicates that lactoferrin inhibits allergen-induced inflammation that is not induced by an endotoxin, such as lipopolysaccharide (LPS). Teng et al. teaches the use of lactoferrin as a treatment for **bacterial and viral infections** (see page 4, lines 21-30 and page 13, lines 1-5). Britigan et al. also teaches the use of lactoferrin to treat **bacterial infections** via scavenging free radicals that are produced by phagocytosis. In fact, Britigan et al. further suggests that lactoferrin may play a role in ameliorating LPS-induced toxicity (see page 151, last sentence of summary). Thus, Applicants assert that the combination of Teng et al. and Britigan et al. teach the **antimicrobial activity of lactoferrin** (lactoferrin's activity against a pathogen), however, the references do not teach or suggest the use of lactoferrin to treat an allergen-induced immune response (lactoferrin's activity against an innocuous agent). Thus, Applicants assert that it would not be obvious to one of skill in the art in view of Teng et al. and Britigan et al. that lactoferrin could be used to treat an immune response that is induced from a non-toxic or innocuous agent.

Still further, Applicants remind the Examiner that to establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). The present claims clearly provide the limitation that lactoferrin is administered to a mammal **that is exposed to an allergen.** Neither Teng et al. nor Britigan et al. teach the limitation that the mammal is exposed to an allergen, thus, Teng et al. and Britigan et al. can not be used to establish *prima facie* obviousness.

Morinaga Milk Inc. teaches a drug composition in the first paragraph that comprises a **mixture of substances**. The substances include lactoferrin, hydrolysed products of lactoferrin, peptides separated from the hydrolysed lactoferrin, synthetic peptides with identical amino acid sequence as hydrolysed lactoferrin peptide and its derivatives, or lactoperoxidase. Thus, Morinaga Milk Inc. only teaches and suggests using **a mixture of substances**; it does not teach using a composition consisting essentially of **lactoferrin and a pharmaceutically acceptable carrier** to treat allergic dermatitis, etc. Morinaga Milk Inc. at best may teach treating allergic dermatitis, however, it does not teach administering **a composition consisting essentially of lactoferrin and a pharmaceutically acceptable carrier** to treat allergic dermatitis. Thus, Morinaga Milk Inc. does not suggest that lactoferrin can be used to treat allergic dermatitis. Since a composition of **mixture of substances** is used in Morinaga Milk Inc., Applicants assert that this reference does not remedy the defeats of Teng et al. and Britigan et al. to establish *prima facie* obviousness in view of the currently amended claims.

De Lacharriere is cited for teaching the use of TNF α antagonists in pharmaceutical compositions. De Lacharriere does not describe that lactoferrin is a TNF antagonist. In fact, the term "TNF α antagonists" is defined purely in functional terms, see column 3 lines 4-10 of the De Lacharriere patent. It is stated that "all substances capable of inhibiting the release and/or synthesis and/or receptor binding of ...TNF alpha" are considered "TNF α antagonists." Without teaching the structures of potential TNF α antagonists, no one in the art would know how to select a candidate from millions of natural and recombinant biological molecules in order to test for its ability to inhibit TNF α production. Such a general statement in De Lacharriere cannot be fairly construed as providing a suggestion for one skilled in the art to select lactoferrin, and specifically, to test its ability to inhibit TNF α production in

dermal cells, and to conduct the test under the particular condition that the mammal has been inflicted with an allergen.

Still further, the Examiner indicates that the claims of De Lacharriere teaches the usefulness of TNF α antagonists, in particular lactoferrin. The only citation of lactoferrin that Applicants can find in De Lacharriere occurs within the claims, which teach the use of a TNF α antagonist, such as lactoferrin, in combination with a compound that produces an irritant side effect. Thus, neither De Lacharriere nor Morinaga Milk Inc. teach or suggest the use of lactoferrin to treat an allergen induced inflammatory response. Since a composition of a mixture of substances is used in Morinaga Milk Inc. and De Lacharriere, Applicants assert that these references do not remedy the defeats of Teng et al. and Britigan et al. to establish *prima facie* obviousness in view of the currently amended claims.

Applicants contend that the teachings of Teng et al., Britigan et al., Morinaga Milk Inc. and De Lacharriere alone or in combination do not teach nor suggest administering lactoferrin alone to a mammal that is exposed to an allergen to treat an allergen-induced inflammatory response. Thus, with the lack of teaching or suggestion, Applicants assert that the references do not meet the basic requirements of a *prima facie* case of obvious and respectfully request that the rejection be withdrawn.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. 102311629 from which the undersigned is authorized to draw.

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Respectfully submitted,

By _____

Melissa W. Acosta
Registration No.: 45,872
FULBRIGHT & JAWORSKI L.L.P.
1301 McKinney, Suite 5100
Houston, Texas 77010-3095
(713) 651-5151
(713) 651-5246 (Fax)